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=> d his

     (FILE 'HOME' ENTERED AT 09:30:51 ON 01 APR 2008)

     FILE 'REGISTRY' ENTERED AT 09:31:10 ON 01 APR 2008
L1             STRUCTURE UPLOADED
L2              42 S L1
L3               1 S L2 AND 6-7/SZ
L4             849 S L1 SSS FUL
L5              48 S L4 AND 6-7/SZ
L6             132 S L4 AND 5-6-7/SZ

     FILE 'CAPLUS' ENTERED AT 09:38:06 ON 01 APR 2008
L7              20 S L5

     FILE 'REGISTRY' ENTERED AT 09:38:56 ON 01 APR 2008
L8               1 S 132539-06-1/RN
L9              94 S 132539-06-1/CRN

     FILE 'CAPLUS' ENTERED AT 09:39:24 ON 01 APR 2008
L10           2364 S L8
L11             62 S L9
L12              5 S L7 AND L10
L13              2 S L7 AND L11
L14              5 S L12 OR L13

=> d l1
L1 HAS NO ANSWERS
L1                STR
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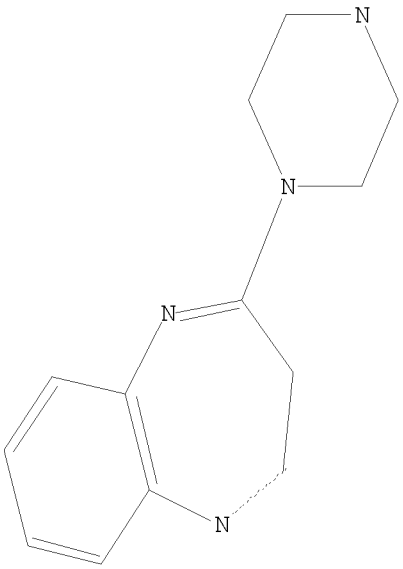


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Structure attributes must be viewed using STN Express query preparation.

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L14 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1066872 CAPLUS
DOCUMENT NUMBER: 145:419187
TITLE: Use of n-desmethylclozapine and related compounds as dopamine stabilizing agents useful in the treatment of neuropsychiatric disease
INVENTOR(S): Burstein, Ethan S.
PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 198pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006107948	A2	20061012	WO 2006-US12463	20060403
WO 2006107948	A3	20061214		
WO 2006107948	A9	20070222		
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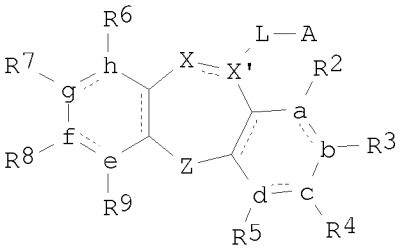
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006231497	A2	20061012	AU 2006-231497	20060403
AU 2006231497	A1	20061012		
CA 2599922	A1	20061012	CA 2006-2599922	20060403
US 20060252744	A1	20061109	US 2006-397248	20060403
EP 1865962	A2	20071219	EP 2006-749226	20060403
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.:
US 2005-668295P P 20050404
US 2005-730193P P 20051025
WO 2006-US12463 W 20060403

OTHER SOURCE(S): MARPAT 145:419187
GI



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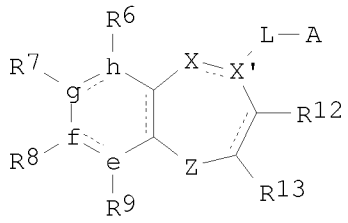

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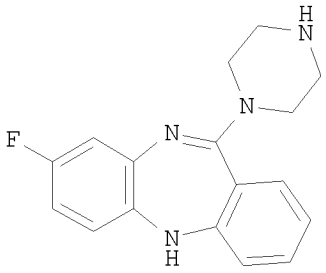


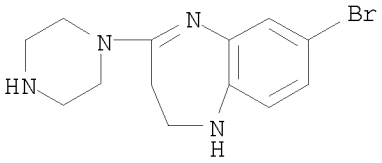
III

AB Disclosed is the use of N-desmethylclozapine (NDMC) and related compds. of formula I and II, to treat a variety of neuropsychiatric diseases including psychosis. It is shown that NDMC and related compds. are agonists or partial agonists at D2 and D3 dopamine receptors and thus may be effective as a dopamine stabilizing agent, allowing it to be used to treat or provide reduced incidence of Extrapyramidal symptoms (EPS) and/or tardive dyskinesias (TD). Also disclosed is administering NDMC and related compds. in combination with other anti-psychotic agents. Compds. of formula I and II wherein A is (un)substituted heterocycle; dotted lines is single and double bonds; X is N, CH, and CH2; X' is C and CH; L is absent, NH(CH2)n, and (CH2)n; n is 0 - 4; a, b, c, d, e, f, g, and h are independently C, N, O, and S, etc.; R2 - R9, R12 and R13 are independently H, halo, (un)substituted C1-6 alkyl(oxy), (un)substituted C2-6 alkenyl, (un)substituted C2-6 alkynyl, CN, NO2, perhaloalkyl, etc.; Z is NH and derivs, O, S and CH2; and their pharmaceutically acceptable salts, esters, amides, and prodrugs thereof are claimed. Example compound III was prepared by cyclization of 2,5-difluoronitrobenzene with 2-aminobenzoic acid followed by amination with piperazine. All the invention compds. were evaluated for their intrinsic activity at human D2 and D3 dopamine receptors. From the assay, it was determined that compound III exhibited pKi of
5.6 and 170 % basal response at D2 dopamine receptor.

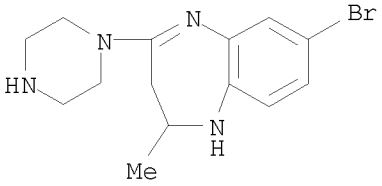
IT 858670-91-4P 858670-92-5P 858670-93-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of n-desmethylclozapine and related compds. as dopamine stabilizing agents and use for treatment of neuropsychiatric diseases)

RN 858670-91-4 CAPLUS

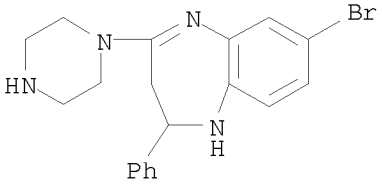
CN 1H-1,5-Benzodiazepine, 7-bromo-2,3-dihydro-4-(1-piperazinyl)- (CA INDEX NAME)



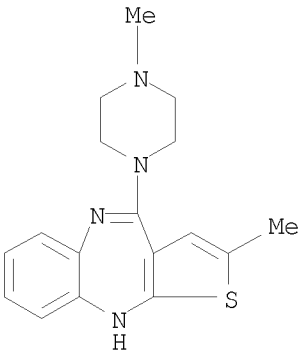
RN 858670-92-5 CAPLUS
CN 1H-1,5-Benzodiazepine, 7-bromo-2,3-dihydro-2-methyl-4-(1-piperazinyl)-
(CA INDEX NAME)



RN 858670-93-6 CAPLUS
CN 1H-1,5-Benzodiazepine, 7-bromo-2,3-dihydro-2-phenyl-4-(1-piperazinyl)-
(CA INDEX NAME)



IT 132539-06-1, Olanzapine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(drug candidate; preparation of n-desmethylclozapine and related compds. as
dopamine stabilizing agents and use for treatment of neuropsychiatric
diseases)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
(CA INDEX NAME)


Me
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Me
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H

L14 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:101681 CAPLUS
DOCUMENT NUMBER: 144:177425
TITLE: Olanzapine salts and their conversion to olanzapine free base
INVENTOR(S): Simonic, Igor; Lenarsic, Roman; Kotar-Jordan, Berta; Zupet, Rok; Gnidovec, Joze
PATENT ASSIGNEE(S): Krka, Tovarna Zdravil, D.D., Novo Mesto, Slovenia
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

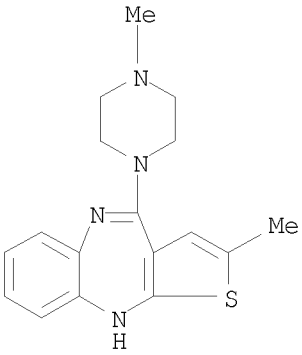
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010620	A2	20060202	WO 2005-EP8218	20050728
WO 2006010620	A3	20060608		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
SI 21850	A	20060228	SI 2004-219	20040728
EP 1781665	A2	20070509	EP 2005-779020	20050728
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: SI 2004-219 A 20040728
WO 2005-EP8218 W 20050728

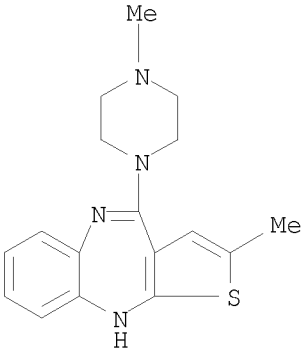
AB The present invention provides olanzapine salts useful as intermediates in the isolation of olanzapine from complex reaction mixts. These salts can be used for the production of olanzapine base which has a suitable purity for pharmaceutical use and can easily be converted to anhydrous olanzapine polymorphic form I, in high yields. Salts such as acetate, benzoate, dihydrochloride and solvates such as mixed water-isopropanol and dichloromethane were prepared

IT 132539-06-1P, Olanzapine 783334-35-0P
861390-70-7P 861452-94-0P 869190-05-6P
874363-46-9P 874363-47-0P 874363-48-1P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of olanzapine form I from olanzapine salts)

RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 783334-35-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, hydrochloride (1:2) (CA INDEX NAME)

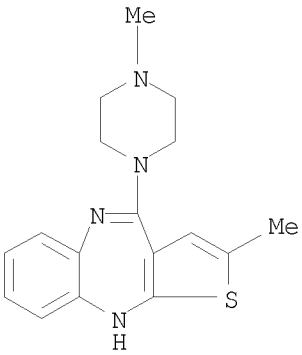


●2 HCl

RN 861390-70-7 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, benzoate (1:1) (CA INDEX NAME)

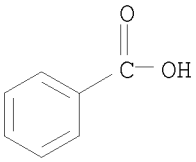
CM 1

CRN 132539-06-1
CMF C17 H20 N4 S



CM 2

CRN 65-85-0
CMF C7 H6 O2



RN 861452-94-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, acetate (9CI) (CA INDEX NAME)

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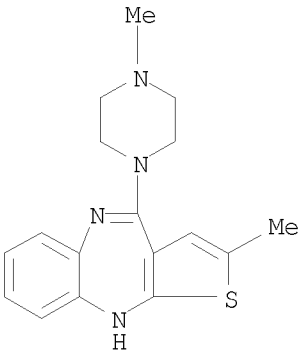
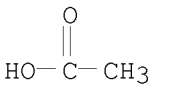
CRN 132539-06-1
CMF C17 H20 N4 S



CM 2

CRN 64-19-7
CMF C2 H4 O2



RN 869190-05-6 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, compd. with dichloromethane (9CI) (CA INDEX NAME)

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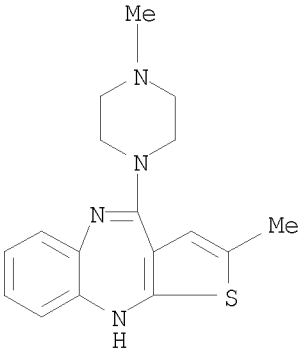
CRN 132539-06-1
CMF C17 H20 N4 S



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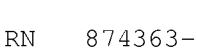
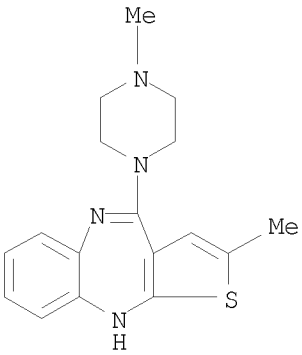


RN 874363-46-9 CAPLUS
CN 2-Propanol, compd. with 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine, hydrate (9CI) (CA INDEX NAME)

CM 1

CRN 132539-06-1
CMF C17 H20 N4 S



CM 2

CRN 67-63-0
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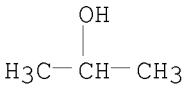
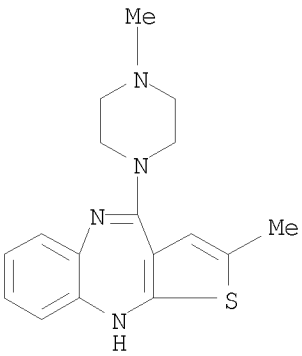


RN 874363-47-0 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, benzenesulfonate (9CI) (CA INDEX NAME)

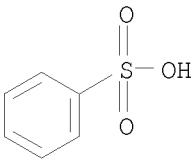
CM 1

CRN 132539-06-1
CMF C17 H20 N4 S



CM 2

CRN 98-11-3
CMF C6 H6 O3 S



RN 874363-48-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, perchlorate (9CI) (CA INDEX NAME)

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CRN 132539-06-1
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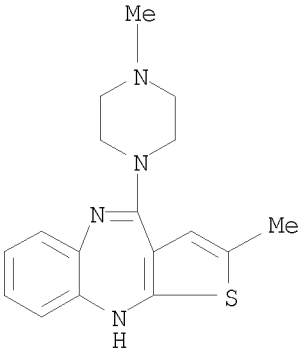
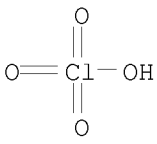
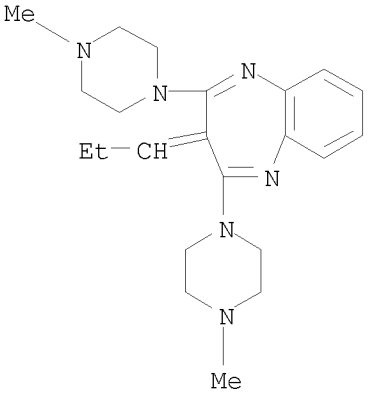


CM 2

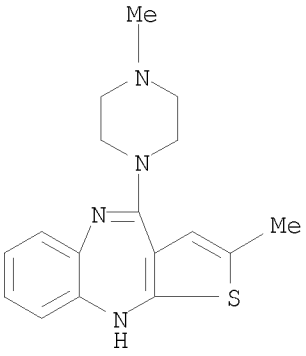
CRN 7601-90-3
CMF Cl H O4



IT 733811-11-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of olanzapine form I from olanzapine salts)
RN 733811-11-5 CAPLUS
CN 3H-1,5-Benzodiazepine, 2,4-bis(4-methyl-1-piperazinyl)-3-propylidene- (CA INDEX NAME)



IT 783334-36-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of olanzapine form I from olanzapine salts)
RN 783334-36-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L14 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1004752 CAPLUS
DOCUMENT NUMBER: 143:311947
TITLE: Isopropanol water solvate of olanzapine
INVENTOR(S): Kotar-Jordan, Berta; Lenarsic, Roman; Grcman, Marija; Smrkolj, Matej; Meden, Anton; Simonic, Igor; Zupet, Rok; Gnidovec, Joze; Benkic, Primoz
PATENT ASSIGNEE(S): Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085256	A1	20050915	WO 2005-EP2389	20050307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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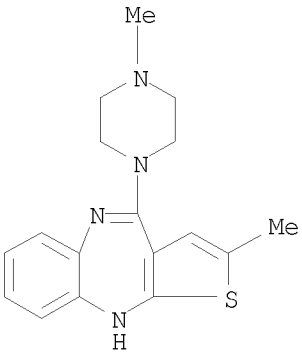
DE 102004060412	A1	20060706	DE 2004-102004060412	20041214
CA 2557986	A1	20050915	CA 2005-2557986	20050307
EP 1730153	A1	20061213	EP 2005-707723	20050307
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
NO 2006004484	A	20061129	NO 2006-4484	20061003
IN 2006CN03716	A	20070615	IN 2006-CN3716	20061009
US 20070191348	A1	20070816	US 2006-591831	20061023

PRIORITY APPLN. INFO.:		
SI 2004-73	A	20040308
DE 2004-102004060412	A	20041214
WO 2005-EP2389	W	20050307

AB The invention relates to a novel and well defined solvate form of olanzapine which contains 2 mols. of water and 1 mol. of isopropanol per 2 mols. of olanzapine, and which can be converted into other, forms of olanzapine, in particular form I of olanzapine, as well as processes for preparing form I olanzapine.
IT 864743-41-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(olanzapine solvate; prepn of isopropanol water solvates of olanzapine)
RN 864743-41-9 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-, compd. with 2-propanol (2:1), dihydrate (9CI) (CA INDEX NAME)

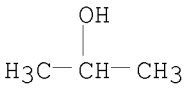
CM 1

CRN 132539-06-1
CMF C17 H20 N4 S

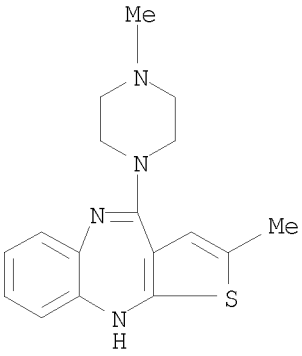


CM 2

CRN 67-63-0
CMF C3 H8 O

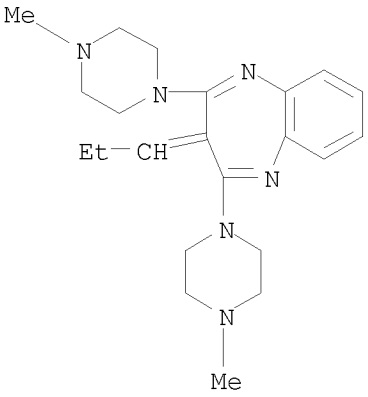


IT 132539-06-1, Olanzapine
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(polymorphism; prepn of isopropanol water solvates of olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

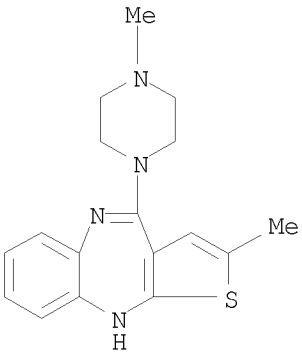


IT 733811-11-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn of isopropanol water solvates of olanzapine)
RN 733811-11-5 CAPLUS

CN 3H-1,5-Benzodiazepine, 2,4-bis(4-methyl-1-piperazinyl)-3-propylidene- (CA INDEX NAME)



IT 132539-06-1DP, Olanzapine, methylene chloride hemisolvate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn of isopropanol water solvates of olanzapine)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn of isopropanol water solvates of olanzapine

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:612094 CAPLUS
DOCUMENT NUMBER: 143:133403
TITLE: Amino-substituted diaryl[a,d]cycloheptene analogs as muscarinic agonists, their preparation and use in the treatment of neuropsychiatric disorders
INVENTOR(S): Ek, Fredrik; Olsson, Roger; Ohlsson, Joergen
PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005063254	A2	20050714	WO 2004-US43224	20041221
WO 2005063254	A3	20050915		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004308955	A1	20050714	AU 2004-308955	20041221
CA 2550735	A1	20050714	CA 2004-2550735	20041221
US 20050192268	A1	20050901	US 2004-19555	20041221
EP 1696931	A2	20060906	EP 2004-815318	20041221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1913900	A	20070214	CN 2004-80041356	20041221
BR 2004017749	A	20070410	BR 2004-17749	20041221
SG 133606	A1	20070730	SG 2007-4645	20041221
JP 2007534656	T	20071129	JP 2006-547344	20041221
US 20060194784	A1	20060831	US 2006-417441	20060503
US 20060199798	A1	20060907	US 2006-417859	20060503
MX 2006PA07244	A	20060818	MX 2006-PA7244	20060621
NO 2006003371	A	20060922	NO 2006-3371	20060720
IN 2006KN02041	A	20070518	IN 2006-KN2041	20060720
US 20070197502	A1	20070823	US 2007-733476	20070410

PRIORITY APPLN. INFO.:		
US 2003-531927P	P	20031222
US 2004-548090P	P	20040224
US 2004-548604P	P	20040227
US 2004-19555	A1	20041221
WO 2004-US43224	W	20041221

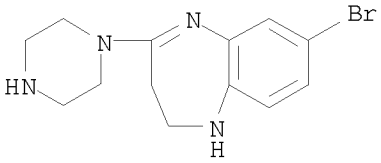
OTHER SOURCE(S): CASREACT 143:133403; MARPAT 143:133403
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

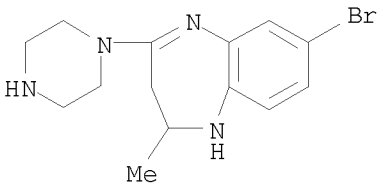
AB The invention relates to a group of novel amino-substituted dibenzazepines I, benzazepines II and related clozapine analogs, which are agonists of muscarinic receptors. In compds. I and II, W is N, CH, O, or S; Y is N, O, or CH; R1, R6, and R7 are independently absent or selected from H, halo, amino, (un)substituted C1-20 alkyl, (un)substituted C3-8 cycloalkyl, (un)substituted aryl, etc., or R1R6 is -CH2CH2-; each R2, R3, R4, and R5 is independently selected from H, halo, (un)substituted C1-6 alkyl, (un)substituted C1-6 alkoxy, cyano, etc., or R2 and R3, or R3 and R4, or R4 and R5 taken together, along with the ring carbons to which they are attached, form a 5- or 6-membered cycloalkyl, heterocyclyl or heteroaryl ring, or a 6-membered aryl ring; Z is (un)substituted NH, O, S, or CH2; and R8 and R9 are independently selected from H, halo, (un)substituted C1-6 alkyl, (un)substituted C1-6 alkoxy, cyano, etc., or R8 and R9 taken together, along with the ring carbons to which they are attached, form a 5- or 6-membered cycloalkyl, heterocyclyl or heteroaryl ring, or a 6-membered aryl ring; including pharmaceutically acceptable salts, esters, amides or prodrugs of these, provided that compound I is not clozapine or N-desmethylclozapine. The invention also relates to the preparation of I, preparation of a combinatorial library of compds. I, pharmaceutical compns. containing compound I with a physiol. acceptable carrier, diluent, or excipient, optionally including a neuropsychiatric agent as well as to the use of the compns. for treating neuropsychiatric disorders. Substitution of 4-chloro-2-fluoronitrobenzene with 2-amino-5-chlorobenzoic acid followed by reduction of the nitro group, ring-closing coupling, and condensation with piperazine gave dibenzodiazepine III. The compds. of the invention express efficacy (eff) at muscarinic M1 receptors in the range of -11 to 92 and potency (expressed as pEC50) of 5.5 to 7.2; the compds. had eff at M2 receptors of -14 to 187 and pEC50 of 5.4 to 6.6.

IT 858670-91-4P 858670-92-5P 858670-93-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of amino-substituted diarylcycloheptene analogs as muscarinic agonists and methods of treatment of neuropsychiatric disorders)

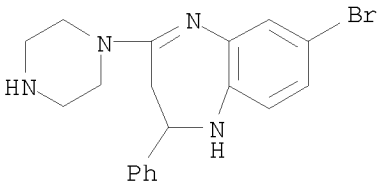
RN 858670-91-4 CAPLUS
CN 1H-1,5-Benzodiazepine, 7-bromo-2,3-dihydro-4-(1-piperazinyl)- (CA INDEX NAME)



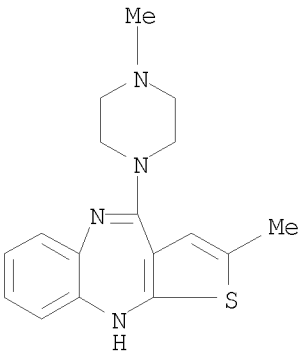
RN 858670-92-5 CAPLUS
CN 1H-1,5-Benzodiazepine, 7-bromo-2,3-dihydro-2-methyl-4-(1-piperazinyl)- (CA INDEX NAME)



RN 858670-93-6 CAPLUS
CN 1H-1,5-Benzodiazepine, 7-bromo-2,3-dihydro-2-phenyl-4-(1-piperazinyl)-
(CA INDEX NAME)



IT 132539-06-1, Olanzapine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of amino-substituted diarylcycloheptene analogs as muscarinic agonists and methods of treatment of neuropsychiatric disorders)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
(CA INDEX NAME)

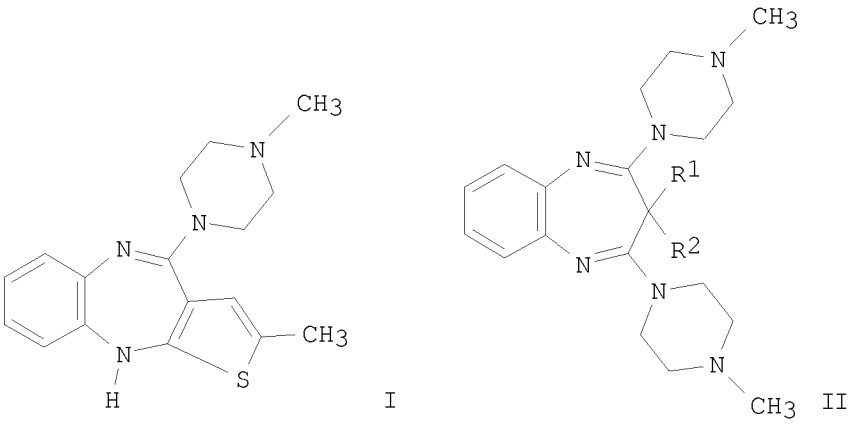


L14 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:633931 CAPLUS
DOCUMENT NUMBER: 141:174199
TITLE: Process and symmetrical bispiperazinylbenzodiazepine intermediates for the preparation of olanzapine
INVENTOR(S): Lenarsic, Roman; Zupet, Rok; Benedik, Milena; Mohar, Barbara
PATENT ASSIGNEE(S): Krka Tovarna Zdravil, D.D. Novo Mesto, Slovenia
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004065390	A1	20040805	WO 2004-EP299	20040116
WO 2004065390	A8	20041216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ				
DE 10301923	B3	20040916	DE 2003-10301923	20030117
EP 1594879	A1	20051116	EP 2004-702675	20040116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060040921	A1	20060223	US 2005-541604	20050707
NO 2005003829	A	20051012	NO 2005-3829	20050815

PRIORITY APPLN. INFO.:			
	DE 2003-10301923	A	20030117
	WO 2004-EP299	W	20040116

OTHER SOURCE(S): MARPAT 141:174199
GI

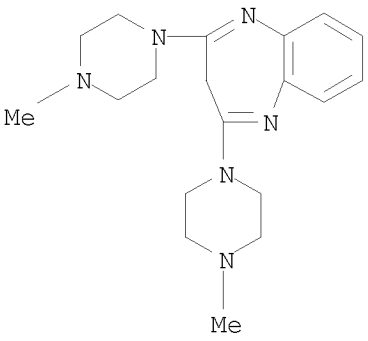


AB The invention provides an improved process for preparing olanzapine (I) or its salts via intermediates II [R1, R2 = CHC2H5; R1 = H, R2 = H or

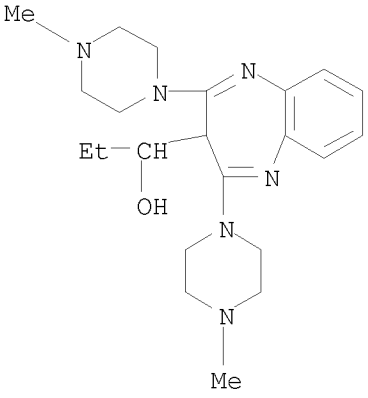
-CH(OR3)C2H5; R3 = H, acyl, sulfonyl] and their salts. Several intermediates II are also claimed per se. Thus, 3H-[1,5]benzodiazepine-2,4-diamine was heated with 1-methylpiperazine in DMSO/toluene to give II (R1 = R2 = H) (82%), which was deprotonated with LDA followed by the addition of propionaldehyde to afford propanol II (R1 = H, R2 = -CH(OH)C2H5). This alc. could be directly acylated with trifluoroacetic acid anhydride without purification, and was further converted to alkene II (R1 and R2 together form =CHC2H5) under stirring with NaOH (89% for 3 steps). Subsequent treatment of this intermediate with sulfur in the presence of pyridinium p-toluenesulfonate in DMSO/1-propanol delivered olanzapine in 66.6% yield. One of the key advantages of the process is the use of intermediate II (R1 and R2 together form =CHC2H5) as starting material in the final step, which is sym. and therefore the possibility of obtaining undersired regioisomers is excluded.

IT 733811-07-9P 733811-09-1P 733811-11-5P
733811-13-7P 733811-15-9P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of olanzapine via sym. bispiperazinylbenzodiazepine intermediates)

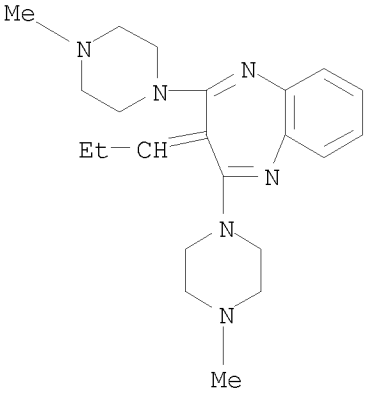
RN 733811-07-9 CAPLUS
CN 3H-1,5-Benzodiazepine, 2,4-bis(4-methyl-1-piperazinyl)- (CA INDEX NAME)



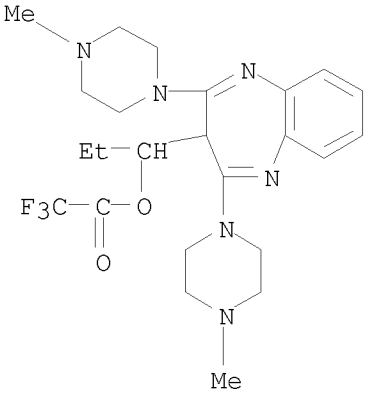
RN 733811-09-1 CAPLUS
CN 3H-1,5-Benzodiazepine-3-methanol, α-ethyl-2,4-bis(4-methyl-1-piperazinyl)- (CA INDEX NAME)



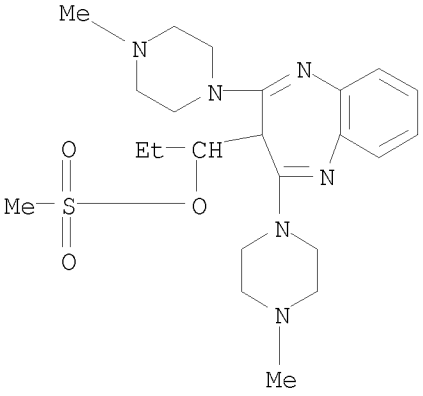
RN 733811-11-5 CAPLUS
CN 3H-1,5-Benzodiazepine, 2,4-bis(4-methyl-1-piperazinyl)-3-propylidene- (CA INDEX NAME)



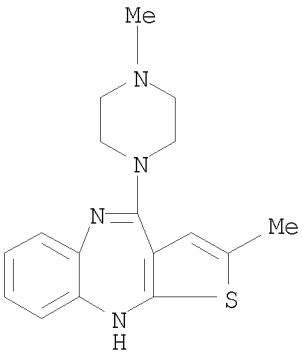
RN 733811-13-7 CAPLUS
CN Acetic acid, trifluoro-, 1-[2,4-bis(4-methyl-1-piperazinyl)-3H-1,5-benzodiazepin-3-yl]propyl ester (9CI) (CA INDEX NAME)



RN 733811-15-9 CAPLUS
CN 3H-1,5-Benzodiazepine-3-methanol, α-ethyl-2,4-bis(4-methyl-1-piperazinyl)-, methanesulfonate (ester) (9CI) (CA INDEX NAME)



IT 132539-06-1P, Olanzapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of olanzapine via sym. bispiperazinylbenzodiazepine intermediates)
RN 132539-06-1 CAPLUS
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L1             STRUCTURE UPLOADED
L2           42 S L1
L3            1 S L2 AND 6-7/SZ
L4          849 S L1 SSS FUL
L5           48 S L4 AND 6-7/SZ
L6          132 S L4 AND 5-6-7/SZ

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L7           20 S L5

     FILE 'REGISTRY' ENTERED AT 09:38:56 ON 01 APR 2008
L8            1 S 132539-06-1/RN
L9           94 S 132539-06-1/CRN

     FILE 'CAPLUS' ENTERED AT 09:39:24 ON 01 APR 2008
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L11          62 S L9
L12           5 S L7 AND L10
L13           2 S L7 AND L11
L14           5 S L12 OR L13

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     FILE 'REGISTRY' ENTERED AT 09:42:33 ON 01 APR 2008
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L16       30251 S >1 46.383/RID
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L18         256 S C23 H32 N6 O4/MF OR C19 H28 N6/MF
L19           4 S L17 NOT L18
L20          44 S L5 NOT L19

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L21           3 S L19
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